In a further aspect of the invention, the concentrates may be used as an infusate in hemodialysis. Consequently, the present invention provides a use of a sterile calcium-free concentrate according to the first embodiment for preparing an infusate for hemofiltration, where said concentrate comprises sodium chloride (NaCl) 90.72 ± 9.0 g/l, magnesium chloride (MgCl2) ~~2.05 ± 0.2 g/l~~ **0.96 ± 0.09 g/l**, and sodium bicarbonate (NaHCO3) 28.35 ± 2.8 g/l. The present invention also provides a method for hemofiltration comprising administering a sterile dialysis solution comprising Na 140 ± 14 mmol/l, Mg 0.75 ± 0.07 mmol/l, Cl 116.5 ± 11 mmol/l, and HCO3 25.0 ± 2.5 mmol/l to a patient in need thereof. The infusate may be prepared by mixing 3000 ml of sterile water to 240 ml of the concentrate.

REMARKS

It was discovered during the prosecution in Europe that the original range for magnesium specified as 2.05 ± 0.2 g/l in the disclosure and original claim 1 was an inadvertent error and in fact should clearly be 0.96 ± 0.09 g/l. This correction is requested on the grounds that the inadvertent error would immediately be evident to a person skilled in the art as well as the proper correction required on the following basis.

It would be immediately evident to a skilled person that there must be a direct relationship between the concentration of each component in the dialysis concentrate and the ion components in the diluted dialysis solution.

In order to achieve a preferred bicarbonate concentration of 25.0 ± 2.5 mmol/L in the dialysis solutions, the dialysis concentrate containing 28.3 ± 2.8 g/l sodium bicarbonate must be diluted by a factor of 13.5. This is entirely consistent with the teaching of the specification at page 13, lines 12-13, where 80ml of bicarbonate concentrate is added to a litre of water to make 1080 ml dialysate, and at page 13, lines 3-6 where one 240 ml unit of concentrate is diluted with 3 litres of water or other suitable diluent.

However, in order for the dialysis solution to have a magnesium concentration of 0.75 ± 0.07 mmol/L, which is expressly stated in the specification at page 2, lines 19-21 and to be variable within only a narrow range, the concentrate must correctly contain magnesium chloride at a concentration of 0.96 ± 0.09 g/l, not 2.05 ± 0.2 g/l.

Thus, not only would this inadvertent error in the calculation of the magnesium chloride concentration in the concentrate have been immediately evident to the skilled person, but also it would have been immediately evident what the correct concentration should be in order to achieve the required magnesium concentration in the diluted dialysis concentrate. Please be advised that this correction was approved in Europe and may be pursued in Canada.

For example to be specific knowing that it is desired to have .75 mmol/l of magnesium in the dialysis solution the following would be the correct simple calculation evident to one skilled in the art to determine the required amount of MgCl2 in the dialysis solution. The molecular weight of MgCl2 is 95.21 as determined from the attached periodic table from the Merck Index.

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Therefore: $.75 \frac{mmol}{L} \times 1.08L = 0.81$ mmol

- 0.81 mmol is 8.1×10^{-4} mol
- but MgCl2 has a molecular weight of $\frac{95.21g}{mol}$
- 8.1×10^{-4} mol x 95.21 g/mol = 7.71×10^{-2} g
- to convert this value to g/l divide this value by 80ml of concentrate
- $\frac{7.71 \times 10^{-2}\,g}{.08L} = 0.96375$ g/l rounded to 0.96 plus or minus 10%

Clearly therefore by simple calculations and using the periodic table to determine molecular weights the original valve of 2.05 ± 10% is clearly incorrect and an inadvertent error.

To verify that this simple calculation was carried out for determination of bicarbonate the same simple calculation is repeated below.

Therefore: $\frac{25.0\ mmol}{L} \times 1.08L = 27$ mmol

27 mmol is 2.7×10^{-2} mol but NaHCO3 has a molecular weight of 84 g/mol

2.7×10^{-2} mol x 84 g/mol = 2.268 g

$\frac{2.268\ g}{.08L} = 28.35$ g/l ± 10% required in concentrate

This value was correctly stated in the disclosure using the same method.

Further to verify that this simple calculation was carried out properly for determination of chloride a similar mass balance calculation was done. These calculations are included in the attached work sheet.

In determination of chloride in a dialysis solutions one needs to consider the levels of Sodium Chloride and Magnesium Chloride which are both sources of chloride. As determined in the work sheet the numbers specified for NaCl and $MgCl_2$ in the concentrate and the ions in the dialysis solution are accurate only if the Mg valve is .96 ± 10% and not 2.05 ± 10%.

Therefore Applicant respectfully requests entry of this Amendment after Allowance on the record, so that the correction may be included with the printed patent. The Examiner is requested to advise the Applicant of his determination.

Should any questions arise, the Examiner is requested to contact Neil H. Hughes at the office of Applicant's Agents, IVOR M. HUGHES, Barrister & Solicitor, Patent & Trademark Agents at area code (925) 771-6414, at his convenience.

Respectfully submitted,

Neil H. Hughes, P.Eng.
Registration No. 33,636
Agent for Applicant

NHH/dj

Enclosures:

1. Periodic Table from the Merck Index.
2. Mass Balance Work Sheet.

Work Sheet

Our Reference No. PT-1946001
Applicants Name: Dialysis Solutions Inc.
Serial No. 10/020,882
Examiners Name: John D. Pak

Mass Balance for the components of dialysis composition.

Concentrate as specified contains:
g/L= gram /Litre
[NaCl] 90.72±9.0 g/L
[$NaHCO_3$] 28.35 ±2.8 g/L
[$MgCl_2$] 0.96±0.9 r/L

Molecular weights (MW): from periodic table in Merck Index specified in grams/mole

[Na] = 22.989768 g/mol
[Cl] = 35.4527 g/mol
[Mg] = 24.3050 g/mol
[HCO_3]= (1.00794+12.011+3*15.9994) = 61.01714 g/mol

To determine the ion concentrations in the dialysis solution
Breaking [NaCl] into its ion components by weight:

[Na] part: 90.72 / (22.989768+35.4527)* 22.989768= 35.68692 g
[Cl] part: 90.72-35.68692= 55.03308g

Breaking [$MgCl_2$] into its ion components by weight:

[Mg] part: 0.96/ (24.3050+35.4527*2)* 24.3050=0.245066g
[Cl] part: 0.96-0.245066=0.7149g

Breaking [$NaHCO_3$] into its ion components by weight:

[Na] part: 28.35/ (22.989768+61.01714)*22.989768=7.758409 g
[HCO_3] part: 28.35-7.758409= 20.5915g

Total Mass of ions per Litre of concentrated solution from above

[Na] : 35.68692 g+7.758409 g=43.44533 g

[Mg] : 0.245066 g

[Cl] : 55.03308g + 0.7149g = 55.74798g

[HCO_3]: 20.5915 g

Using 80 ml (0.08L) of the solution added to 1 Litre of water the following content of in the dialysis solution will be achieved:

$$[\mathrm{Mg}]: \frac{0.245066\ \mathrm{g}/\mathrm{L} * 0.08\ \mathrm{L} * 1000\ \mathrm{mmol/mol}}{1.08\mathrm{L} * 24.3050\mathrm{g/mol}} = 0.746 mmol/L \text{ or } .75 \pm 10\%\ \mathrm{mmol/L}$$

$$[\mathrm{CL}]: \frac{55.74798\ \mathrm{g}/\mathrm{L} * 0.08\ \mathrm{L} * 1000\ \mathrm{mmol/mol}}{1.08\mathrm{L} * 35.4527\mathrm{g/mol}} = 116.48 mmol/L \text{ or } 116 \pm 10\%\ \mathrm{mmol/L}$$

$$[\mathrm{Na}]: \frac{43.44533\ \mathrm{g}/\mathrm{L} * 0.08\ \mathrm{L} * 1000\ \mathrm{mmol/mol}}{1.08\mathrm{L} * 22.989768\mathrm{g/mol}} = 139.98 mmol/L \text{ or } 140 \pm 10\%\ \mathrm{mmol/L}$$

$$[\mathrm{HCO_3}]: \frac{20.5915\ \mathrm{g}/\mathrm{L} * 0.08\ \mathrm{L} * 1000\ \mathrm{mmol/mol}}{1.08\mathrm{L} * 61.01714\mathrm{g/mol}} = 24.998 mmol/L \text{ or } 25 \pm 10\%\ \mathrm{mmol/L}$$

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PERIODIC CHART OF THE ELEMENTS

KEY

Common Oxidation States →	+1 +3	79	← Atomic Number
	Au		← Atomic Symbol
Atomic Weight →	196.966569		
Electron Configuration of Outer Shells →	-32-18-1		

Transition Elements (groups 3/IIIb – 12/IIb)

1/Ia	2/IIa	3/IIIb	4/IVb	5/Vb	6/VIb	7/VIIb	8/VIIIb	9/VIII	10/VIII	11/Ib	12/IIb	13/IIIa	14/IVa	15/Va	16/VIa	17/VIIa	18/VIIIa/0
+1 1 H 1.00794 1																	0 2 He 4.002602 2
+1 3 Li 6.941 2-1	+2 4 Be 9.012182 2-2											+3 5 B 10.811 2-3	+2 ±4 6 C 12.0107 2-4	±1 ±2 ±3 +4 +5 7 N 14.0067 2-5	-2 8 O 15.9994 2-6	-1 9 F 18.9984032 2-7	0 10 Ne 20.1797 2-8
+1 11 Na 22.98976928 2-8-1	+2 12 Mg 24.3050 2-8-2											+3 13 Al 26.9815386 2-8-3	+2 ±4 14 Si 28.0855 2-8-4	±3 +5 15 P 30.973762 2-8-5	+4 +6 -2 16 S 32.065 2-8-6	±1 +5 +7 17 Cl 35.453 2-8-7	0 18 Ar 39.948 2-8-8
+1 19 K 39.0983 -8-8-1	+2 20 Ca 40.078 -8-8-2	+3 21 Sc 44.955912 -8-9-2	+2 +3 +4 22 Ti 47.867 -8-10-2	+2 +3 +4 +5 23 V 50.9415 -8-11-2	+2 +3 +6 24 Cr 51.9961 -8-13-1	+2 +3 +4 +7 25 Mn 54.938045 -8-13-2	+2 +3 26 Fe 55.845 -8-14-2	+2 +3 27 Co 58.933195 -8-15-2	+2 +3 28 Ni 58.6934 -8-16-2	+1 +2 29 Cu 63.546 -8-18-1	+2 30 Zn 65.409 -8-18-2	+3 31 Ga 69.723 -8-18-3	+2 +4 32 Ge 72.64 -8-18-4	±3 +5 33 As 74.92160 -8-18-5	+4 +6 -2 34 Se 78.96 -8-18-6	±1 +5 35 Br 79.904 -8-18-7	0 36 Kr 83.798 -8-18-8
+1 37 Rb 85.4678 -18-8-1	+2 38 Sr 87.62 -18-8-2	+3 39 Y 88.90585 -18-9-2	+4 40 Zr 91.224 -18-10-2	+3 +5 41 Nb 92.90638 -18-12-1	+6 42 Mo 95.94 -18-13-1	+4 +6 +7 43 Tc (97.9072) -18-13-2	+3 44 Ru 101.07 -18-15-1	+3 45 Rh 102.90550 -18-16-1	+2 +4 46 Pd 106.42 -18-18-0	+1 47 Ag 107.8682 -18-18-1	+2 48 Cd 112.411 -18-18-2	+3 49 In 114.818 -18-18-3	+2 +4 50 Sn 118.710 -18-18-4	±3 +5 51 Sb 121.760 -18-18-5	+4 +6 -2 52 Te 127.60 -18-18-6	±1 +5 +7 53 I 126.90447 -18-18-7	0 54 Xe 131.293 -18-18-8
+1 55 Cs 132.9054519 -18-8-1	+2 56 Ba 137.327 -18-8-2	57–71 See Lanthanides	+4 72 Hf 178.49 -32-10-2	+5 73 Ta 180.94788 -32-11-2	+6 74 W 183.84 -32-12-2	+4 +6 +7 75 Re 186.207 -32-13-2	+3 +4 76 Os 190.23 -32-14-2	+3 +4 77 Ir 192.217 -32-15-2	+2 +4 78 Pt 195.084 -32-16-2	+1 +3 79 Au 196.966569 -32-18-1	+1 +2 80 Hg 200.59 -32-18-2	+1 +3 81 Tl 204.3833 -32-18-3	+2 +4 82 Pb 207.2 -32-18-4	+3 +5 83 Bi 208.98040 -32-18-5	+2 +4 84 Po (208.9824) -32-18-6	±1 +5 +7 85 At (209.9871) -32-18-7	0 86 Rn (222.0176) -32-18-8
+1 87 Fr (223.0197) -18-8-1	+2 88 Ra (226.0254) -18-8-2	89–103 See Actinides	+4 104 Rf (261.1088) -32-10-2	105 Db (262.1141) -32-11-2	106 Sg (266.1219) -32-12-2	107 Bh (264.12) -32-13-2	108 Hs -32-14-2	109 Mt (268.1388) -32-15-2	110 Ds	111 Rg (272.1535)	112 *Uub		114 *Uuq		116 *Uuh		Noble Gases

	57–71 / 89–103														
Lanthanides	+3 57 La 138.90547 -18-9-2	+3 +4 58 Ce 140.116 -20-8-2	+3 59 Pr 140.90765 -21-8-2	+3 60 Nd 144.242 -22-8-2	+3 61 Pm (144.9127) -23-8-2	+2 +3 62 Sm 150.36 -24-8-2	+2 +3 63 Eu 151.964 -25-8-2	+3 64 Gd 157.25 -25-9-2	+3 65 Tb 158.92535 -27-8-2	+3 66 Dy 162.500 -28-8-2	+3 67 Ho 164.93032 -29-8-2	+3 68 Er 167.259 -30-8-2	+3 69 Tm 168.93421 -31-8-2	+2 +3 70 Yb 173.04 -32-8-2	+3 71 Lu 174.967 -32-9-2
Actinides	+3 89 Ac (227.0277) -18-9-2	+4 90 Th 232.03806 -18-10-2	+4 +5 91 Pa (231.03588) -20-9-2	+3 +4 +5 +6 92 U 238.02891 -21-9-2	+3 +4 +5 +6 93 Np (237.0482) -22-9-2	+3 +4 +5 +6 94 Pu (244.0642) -24-8-2	+3 +4 +5 +6 95 Am (243.0614) -25-8-2	+3 96 Cm (247.0704) -25-9-2	+3 +4 97 Bk (247.0703) -27-8-2	+3 98 Cf (251.0796) -28-8-2	+3 99 Es (252.0830) -29-8-2	+3 100 Fm (257.0951) -30-8-2	+2 +3 101 Md (258.0984) -31-8-2	+2 +3 102 No (259.1010) -32-8-2	+3 103 Lr (262.1097) -32-9-2

Note: Atomic weights are based on the 2001 IUPAC Atomic Weights of the Elements and the 2005 Revised IUPAC Periodic Table of the Elements. Values in parenthesis are used for certain radioactive elements; this value is the relative atomic mass of the isotope of that element of longest known half life.

Note: Elements with atomic numbers 112 and above have been reported but not fully authenticated.

* Symbols based on IUPAC systematic names.